

Pure Tone Audiometry Evaluation Method Effectiveness in Detecting Hearing Changes Due to Workplace Ototoxicant, Continuous Noise, and Impulse Noise Exposures

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Objectives: The purpose of this retrospective cohort study was to compare the relative risks (RR) of hearing impairment due to co-exposure of continuous noise, impulse noise, metal ototoxicants, and organic solvent ototoxicants using several pure tone audiometry (PTA) evaluation methods.

Design: Noise and ototoxicant exposure and PTA records were extracted from a DoD longitudinal repository and were analyzed for U.S. Air Force personnel ($n = 2372$) at a depot-level aircraft maintenance activity at Tinker Air Force Base, Oklahoma using an historical cohort study design. Eight similar exposure groups based on combinations of ototoxicant and noise exposure were created: (1) Continuous noise (reference group); (2) Continuous noise + Impulse noise; (3) Metal exposure + Continuous noise; (4) Metal exposure + Continuous noise + Impulse noise; (5) Solvent exposure + Continuous noise; (6) Solvent exposure + Continuous noise + Impulse noise; (7) Metal exposure + Solvent exposure + Continuous noise; and (8) Metal exposure + Solvent exposure + Continuous noise + Impulse noise. RR of hearing impairment compared to the Continuous noise-exposed reference group was assessed with five PTA evaluation methods including (1) U.S. Department of Defense (DoD) Significant Threshold Shift (STS), (2) Occupational Safety and Health Administration (OSHA) age-adjusted STS, (3) National Institute for Occupational Safety and Health (NIOSH) STS, (4) NIOSH Material Hearing Impairment, and (5) All Frequency Threshold Average.

Results: Hearing impairment was significantly worse for SEG (2) combined exposure to continuous noise and impulse noise only for the PTA evaluation method (2) OSHA Age Adjusted with an RR of 3.11, [95% confidence interval (CI), 1.16–8.31] and was nearly significantly different using PTA evaluation method (4) NIOSH Material Hearing Impairment with an RR of 3.16 (95% CI, 0.99–10.15). Despite no significant differences for SEGs with an ototoxicant exposure, PTA evaluation method (3) NIOSH STS was most sensitive in detecting hearing changes for SEG (8) Metal exposure + Solvent exposure + Continuous noise + Impulse noise as demonstrated by a RR of 1.12 (95% CI, 0.99–1.27).

Conclusions: Results suggest that a single PTA evaluation technique may not be adequate in fully revealing hearing impairment risk due to all stressors and tailoring the PTA evaluation technique to the hazards present in the workplace could better detect hearing impairment. Additionally, results suggest that PTA may not be effective as the sole technique for evaluating hearing impairment due to ototoxicant exposure with continuous noise co-exposure.

Key words: Continuous noise, Impulse noise, Ototoxicants, Pure tone audiometry.

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INTRODUCTION

Noise-induced hearing loss (NIHL) is a significant concern in the occupational health field due to its irreversible nature and adverse impacts on quality of life for affected individuals. The purpose of the U.S. Department of Defense (DoD 2019) Hearing Conservation Program (HCP) is to mitigate hearing loss by directing HCP enrollment for workers exposed to sound pressure levels above the 8-hour time-weighted average (TWA) of 85 decibels A-weighted (dBA) for continuous noise and 140 peak unweighted pressure (dBP) for impulse noise. A vital component of the DoD HCP program is the requirement to monitor individuals with pure tone audiometry (PTA) to mitigate hearing loss through the determination of significant/standard threshold shifts (STS). Despite these efforts, there is a potential gap in HCP effectiveness because auditory disability may be more complicated than the HCP components that involve only achieving acceptable continuous noise levels <85 dBA, implementation of personal protective equipment, or controlling impulse noise below 140 dBP. As a further complication, growing research indicates ototoxic substances, chemicals that negatively impact the hearing organs, may have combined effects with continuous noise exposure (OSHA 2018). Additional exposure to impulse noise, peak noises that are less than one second in duration (ACGIH 2021), may further increase those combined effects. Therefore, concomitant exposures to continuous noise, impulse noise, and ototoxic substances could potentially lead to more severe hearing impairment beyond continuous noise alone.

Due to the prevalence of high levels of noise in society, continuous noise above 85 dBA has been thoroughly researched and regulated. NIHL is most prevalent in the 3000, 4000, and 6000 Hz frequencies, referred to as the “noise notch”, and then spreads to 1000 and 2000 Hz frequencies (Ackley et al. 2007). This loss is a subtle and gradual process occurring primarily in the first 10 years of exposure (Ackley et al. 2007).

Presbycusis, age-related hearing loss due to degeneration or genetics, is another cause of hearing loss relevant in this investigation but the causes are not well understood (Ackley et al. 2007). Presbycusis typically occurs in individuals older than 60 years, with problems understanding speech being the primary complaint rather than hearing difficulty (Sataloff & Sataloff 2006). Although the Occupational Safety and Health Administration (OSHA) allows for adjusting hearing thresholds to account for age-related declines, age adjusting audiogram results are likely to either over or underestimate hearing loss because these adjustments only reflect the distribution of hearing loss in society at a specific point in time (NIOSH 1998).

Hearing Tests

Despite the various causes of hearing loss, PTA is one of the most common methods of evaluating hearing ability and is a required component of an OSHA compliant HCP. PTA uses reference pressure levels for each center frequency to make an initial diagnosis of hearing sensitivity and potential hearing loss (Roeser et al. 2000). Similar to the concept of dB A-weighting, ear sensitivity varies by frequency, and this variation is used to establish the dB HL at center octave bands from 125 Hz to 8000 Hz (Roeser et al. 2000). An individual's dB HL at evaluated frequencies is defined as a 50% response at the lowest measured dB value in relation to the pressure sensitivity of a normal ear (Roeser et al. 2000).

The current DoD Standard, DoD Instruction (DoDI) 6055.12 HCP (DoD 2019), directs services to establish HCPs in alignment with 29 CFR 1910.95. Additionally, DoDI 6055.12 includes requirements to evaluate the combined effects of ototoxic substances but does not specify methodology or substances of concern. Further, DoDI 6055.12 classifies a significant threshold shift (STS) as an average change of 10 dB or more at 2000, 3000, and 4000 Hz in either ear. This definition is the same as an OSHA STS. An STS on an annual audiogram is considered a PTS if follow-up testing reaffirms the shift, or if the follow-up testing is not conducted within the specified time. It should be noted that currently, requirements to conduct PTA as an element of an HCP is only required when noise is a component of exposure and that the PTA requirement does not extend to ototoxicant exposure where noise exposure is not already present.

Evaluating HCP effectiveness is challenging due to the lack of consensus on how to interpret PTA data and lack of data for nonexposed groups (Masterson et al. 2014; Masterson et al. 2015; Soderlund et al. 2016; Rabinowitz et al. 2018). Regarding PTA data for general industry, 29 CFR 1910.95, U.S. STSs are defined as an average change of 10 dB or more at 2000, 3000, and 4000 Hz in either ear, but, unlike DoD criteria, do not require follow-up audiograms to confirm threshold shifts. Additionally, age-specific corrections for >20-years old to <60-years old is allowed but is not mandated by 29 CFR 1910.95 to account for hearing loss associated with aging. Since 1998, the National Institute for Occupational Safety and Health (NIOSH) has recommended more sensitive measures by defining a NIOSH STS as a 15 dB or higher increase for any frequency at 500, 1000, 2000, 3000, 4000, or 6000 Hz in either ear without age adjustments (NIOSH 1998). Other methods for interpreting PTA data include assessing "material hearing impairment", which averages hearing levels across frequencies for comparison to a specific dB HL value (i.e., >25 dB HL). The threshold for impairment has typically been defined as an average of 25 dB HL across specific frequencies by organizations such as NIOSH, OSHA, and the Environmental Protection Agency (EPA) (NIOSH 1998). Additionally, PTA thresholds could be averaged rather than using the absolute value for all monitored frequencies (i.e., 500–6000 Hz).

Assessing nonmilitary U.S. employers, Masterson et al. (2014) used NIOSH STS, OSHA STS, and OSHA STS-Age Adjusted PTA to identify shift rates between industries defined by North American Industry Classification System (NAICS) codes. The first valid audiogram and last two audiograms per individual were used for this PTA assessment. Despite the usage of nonreference audiograms for the first audiogram, the results

of their research found prevalence rates of 20% NIOSH STS, 14% OSHA STS, and 6% OSHA STS-Age Adjusted hearing impairment during the 2001–2010 study. Additionally, Masterson et al. (2014) noted that relationships between methods and within industries remained consistent for all shift definitions. This consistency infers NIOSH STS methods are likely to identify higher numbers of individuals susceptible to hearing loss (Masterson et al. 2014). This increased sensitivity may be due to the NIOSH STS method accounting for hearing changes over a wider range of frequencies (500 to 6000 Hz) compared to the DoD/OSHA method (2000 to 4000 Hz). Masterson et al. (2015) found a prevalence rate of 18% hearing loss using the NIOSH definition of material hearing impairment (>25 dB HL averaged across 1000, 2000, 3000, and 4000 Hz) when assessing the last audiogram available for individuals submitted for their study from 1981 to 2010. Although there are various methods for detecting hearing loss, the most sensitive method for detecting effects from continuous noise, impulse noise, and ototoxicant exposures is presently unknown.

Ototoxicants

Some investigations indicate exposure to solvents below occupational exposure limits (OELs) could have an adverse effect on hearing. A cross-sectional study of 161 paint manufacturing workers identified a higher prevalence of hearing loss identified with PTA and increased auditory-evoked potential latencies in workers exposed to noise below 85 dBA in combination with ototoxic substance exposure below OELs (Juárez-Pérez et al. 2014). In a cross-sectional study of a fiberglass product manufacturing plant, individuals exposed to styrene concentrations ranging from 10 to 20 ppm in combination with noise levels below 85 dBA had significantly worse hearing loss than a reference group (Morata et al. 2011). However, in the exposure groups where noise exposures exceeded 85 dBA, continuous noise became the primary significant factor in the outcome of hearing loss (Morata et al. 2011). These studies suggest continuous noise exposure damage may mask the potential effect ototoxic solvents have on hearing thresholds. Since ototoxic substance exposure alone is not a requirement for HCP enrollment, personnel exposed to a variety of ototoxicant substances on a daily basis may not be evaluated for shifts in hearing thresholds unless noise is also present and serving as the primary trigger for HCP entry.

Combined exposure to ototoxic solvents and continuous noise has been shown to increase the odds of hearing loss (Sliwiska-Kowalska et al. 2001; Metwally et al. 2012; Hormozi et al. 2017; Dement et al. 2018; Fuente et al. 2018). Solvents primarily impact higher frequencies (i.e., >3000 Hz), but depending on the substance, impacts can begin at middle hearing frequencies (i.e., 1000 Hz) (Sliwiska-Kowalska et al. 2001; Hormozi et al. 2017). Chang et al. (2006) observed in a cross-sectional study of 58 workers that concurrent exposure to noise and toluene resulted in relatively high dB HL thresholds at 1000 and 2000 Hz compared to a noise only reference group. A meta-analysis of 15 studies with 7530 combined subjects indicated a dose-response relationship related to organic solvent mixtures and noise (Hormozi et al. 2017). Compared to a nonexposed reference group, individuals with solvent exposures at half the OEL had an odds ratio (OR) of 1.37 [95% confidence interval (CI), 0.75 to 2.48] of hearing loss, and those exposed to levels higher than the OEL had an OR of 4.51 (95% CI, 3.46 to 5.90) (Hormozi et al. 2017). Increasing

the duration of exposure and the number of solvents present had a similar increase in OR of hearing loss (Hormozi et al. 2017). In particular, exposures lasting less than 5 years resulted in an OR of 1.01 (95% CI, 0.92 to 1.10), indicating exposure durations shorter than this period may not be a significant predictor of hearing loss (Hormozi et al. 2017).

DoD-specific studies suggest a synergistic interaction between noise and ototoxicant substance exposures. Assessing 138 U.S. Air Force subjects, hearing loss odds, defined as a 15 dB shift in either ear at 1000 to 4000 Hz, were calculated for individuals exposed for a minimum of 3 years to noise and 3 years to jet fuel, a complex organic solvent mixture that can potentially include n-hexane, n-heptane, toluene, and xylene (Kaufman et al. 2005). This study reported a 70% increased OR despite organic solvent mixture exposures being estimated below OELs (Kaufman et al. 2005). Evaluating exposures for civilians conducting shipyard work, Schaal et al. (2018) assessed 1266 personnel exposed to high/low concentration combinations of noise, ototoxic solvents, and ototoxic metals. Results identified significantly greater hearing level shifts at 2000 Hz, shifts averaged across 2000 to 4000 Hz, and shifts averaged across 500 to 6000 Hz for high metal/solvent compared to low metal/solvent groups with similar noise exposures (Schaal et al. 2018).

Schaal et al. (2017) conducted a similar study to investigate the association between exposures classified as high for metals, solvents, and noise on permanent threshold shift (PTS) development using DoD STS criteria. A total of 1546 personnel at an industrial shipyard were divided into five exposure groups based on level of concentration: high noise (>85 dBA), high metals (lead, cadmium, and arsenic > OSHA action levels) and high solvents (toluene >20 ppm and xylene >3 ppm). Exposure combinations included the following: high metals/solvents, high metals/noise, high metals/solvents/noise, and a low metals/solvents/noise reference group. Logistic regression indicated high metals/solvents and high metals/solvent/noise groups had significantly greater ORs of 2.4; (95% CI, 1.02 to 2.85) and 1.7 (95% CI, 1.46 to 3.94), respectively, compared to a reference group. Both groups were associated with PTSs, using DoD STS criteria, while controlling for age, gender, and exposure duration. These results suggest simultaneous exposures classified as high for metals and solvents may damage hearing more than noise exposure alone.

Beyond affecting just inner ear structure and function, ototoxic chemicals may affect the connected neural pathways. Dysfunctions of the central auditory nervous system following occupational exposures to ototoxicants have been found. This suggests that hearing loss caused by chemicals can have a more detrimental effect on worker quality of life than just NIHL because sounds may be perceived to be both less loud and distorted (Campo et al. 2013).

The purpose of this investigation was to compare the relative risks of hearing impairment from co-exposure to continuous noise, impulse noise, metal ototoxicants, and solvent ototoxicants compared to a population exposed only to noise. Specifically, researchers sought to evaluate (1) DoD/OSHA STS, (2) OSHA STS age-adjusted, (3) NIOSH material hearing impairment, (4) NIOSH STS, and (5) All Frequency Threshold Average hearing PTA evaluation methods in detecting relative risks associated with combined continuous, impulse, and ototoxicant exposures.

MATERIALS AND METHODS

Study Population

Chemical and physical hazard exposure records and PTA records were assessed for personnel employed at Tinker Air Force Base (AFB), near Oklahoma City, Oklahoma. This base is responsible for maintaining C/KC-135, B-1B, B-52, and E-3 airframes to include full overhaul maintenance, aircraft repairs, engineering services, aircraft modifications, depaint and paint services, and flight testing (USAF 2020). Exposure to ototoxic solvents and metals such as cadmium, lead, toluene, and xylene may occur during such industrial processes as paint removal (sanding and grinding primers and paints containing heavy metals), painting, and fuel system maintenance, among others.

Chemical and physical hazard exposure records were extracted from Defense Occupational and Environmental Health Readiness System–Industrial Hygiene (DOEHRS–IH) and PTA records were extracted from Defense Occupational and Environmental Health Readiness System–Hearing Conservation (DOEHRS–HC). DOEHRS–IH is used to manage occupational and environmental health risk data for service members while DOEHRS–HC is used to collect, maintain, compare, and report hearing conservation, hearing readiness and deployment data for DoD personnel (Defense Health Agency 2018; Defense Health Agency 2019). Because DOEHRS–IH and DOEHRS–HC systems are not directly connected except via an individual's social security number, connecting exposure and hearing data for each individual necessitated establishing a unique personal identifier combined with assigned unique similar exposure group (SEG) identifiers to create individual exposure records for assessment and build exposure group combinations. Individual records were assigned to study SEGs by evaluating exposure to ototoxic substances, continuous noise, and impulse noise.

Chemical and Physical Stressor Results

The ototoxicant substances shown in Table 1 were selected for review in this research based, in part, on OSHA's ototoxic advisory (2018), a review of literature (Campo et al. 2009; Johnson & Morata 2009; Vyskocil et al. 2012), and based on substances commonly found at the maintenance facility.

Exposure record data collection methodology is described in detail by Blair and co-authors (2021). DOEHRS–IH noise and chemical exposure data were collected from January 2005 to October 2019. The basic methodology for creating individual exposure records was derived from assessments and evaluations of occupational hazards assigned to a SEG. Researchers determined SEG exposure to ototoxic metals in the study population consisted of cadmium and lead while ototoxic solvents included benzene, ethyl benzene, toluene, and p-xylene. Chemical exposure evaluations included professional judgment and sampling-based assessments to determine dichotomous (presence or absence) exposure.

Noise exposure was assessed with sound level meters (SLMs) to measure sound pressure levels in dBA or, because noise exposures were not always quantified, qualitative classification was also conducted. The "Analyze Occupational Exposure Hazards" report within DOEHRS–IH determined any SEG exposure to ototoxic substances or continuous noise. This report provided a comprehensive evaluation of SEGs through the usage of professional judgment and sampling-based assessments. The "Installation Noise Sample Log" report provided

TABLE 1. Ototoxic substances

Category	Substance	Threshold Limit Value-Time-Weighted Average	Toxicological Endpoint (Threshold Limit Value Basis)
Metal	Cadmium	0.01 mg/m ³	Kidney damage
Metal	Cadmium compounds	0.002 mg/m ³ (respirable)	
Metal	Germanium dioxide	0.2 ppm	Hematologic effects
Metal	Lead	0.05 mg/m ³	Central nervous system impairment, peripheral nervous system impairment, hematologic effects
Metal	Lead inorganic compounds		
Metal	Mercury	0.01 mg/m ³	Central nervous system impairment, peripheral nervous system impairment, kidney damage
Metal	Tin organic compounds	0.1 mg/m ³	Eye irritation, upper respiratory track irritation, headache, nausea, central nervous system impairment, immune effects
Solvent	Benzene	0.5 ppm	Leukemia
Solvent	Ethyl benzene	*20 ppm	*Upper respiratory track irritation, eye irritation ototoxicity , kidney effects, central nervous system impairment
Solvent	Heptane	400 ppm	Central nervous system impairment, upper respiratory track irritation
Solvent	N-Hexane	50 ppm	Central nervous system impairment, peripheral neuropathy, eye irritation
Solvent	Methyl styrene	10 ppm	Upper respiratory track irritation, kidney damage, female reproductive damage
Solvent	Styrene	10 ppm	Central nervous system impairment, hearing impairment , upper respiratory track irritation, peripheral neuropathy
Solvent	Toluene	20 ppm	Central nervous system impairment, visual impairment, hearing impairment , female reproductive system effects, pregnancy loss
Solvent	Trichloroethylene	10 ppm	Central nervous system impairment, cognitive decrements, renal toxicity
Solvent	P-xylene	*20 ppm	*Eye irritation, upper respiratory track irritation, hematologic effects, ototoxicity , central nervous system impairment

Bold indicates ototoxicant outcome.

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mg/m³, milligrams per cubic meter of air; ppm: parts per million.

SEG exposure information to potential impulse noise sources based on the presence or absence of keywords in the survey's qualitative description. This report provided data for individual equipment assessed at a location by SLM with dBA measurements and qualitative classification of the source as "continuous," "impact/impulse," or "intermittent." Keywords in the IH survey's qualitative description including "rivet," "shear," and "impact" were used to distinguish between continuous noise exposure and impulse/impact noise. These terms were used specifically since the sources were commonly found at this maintenance facility.

In workplaces where ototoxicants and noise sources were determined to be present, the industrial hygienist may have chosen to quantify exposures with air sampling and noise measurements. However, there may have been situations where noise and ototoxicant exposures were present in the workplace but exposure was not quantified. This may have been a result of a determination that the exposure did not present a substantial health risk. These qualitative exposure assessment decisions were documented in DOEHS-IH and considered such information as frequency and duration of exposure. Dichotomous exposure criteria to at least one substance per category and for at least 3 years were used to place personnel in an exposure category. If SEG assignment did not meet these criteria, then personnel were classified as not being exposed.

PTA Results

PTA results were assessed for civilian personnel employed by Tinker AFB from January 2005 to July 2019. Hearing threshold shifts were determined by comparing an individual's first audiogram record and final audiogram record to

calculate a threshold shift record at each frequency. Exclusion criteria and excluded personnel groups included the following: any audiogram records with missing hearing test data (at any frequency), personnel with multiple birthdates in the database (indicative of data entry error), declared ear nose throat (ENT) problems, values <−10 or >100 dB HL, <3 years difference between first and last audiogram, and military service members because of anticipated short duration exposures. Military service members tend to be moved to different bases frequently and are also either promoted to higher, more administrative duties, or separated from the service. Civilian employees tend to have a more stable occupational exposure history.

Researchers evaluated the relative risk of hearing loss by study exposure group. Researchers calculated RRs for the development of hearing loss using several PTA evaluation methods (Table 2). (1) DoD/OSHA STS: ≥10 dB HL threshold shift average shift at 2000, 3000, 4000 Hz; (2) OSHA STS age-adjusted: ≥10 dB HL threshold shift age-adjusted average shift at 2000, 3000, 4000 Hz; (3) NIOSH STS: ≥15 dB HL threshold shift for either ear at any frequency 500, 1000, 2000, 3000, 4000, 6000 Hz; (4) NIOSH Material Hearing Impairment: >25 dB HL threshold average for both ears at 1000, 2000, 3000, 4000 Hz; and (5) All Frequency Threshold Average 500–6000 Hz: ≥25 dB HL threshold average at 500, 1000, 2000, 3000, 4000, 6000 Hz.

Statistical Analysis

Microsoft Access (Microsoft, Redmond, WA) was used to count unique entries that met PTA test conditions and to

TABLE 2. Pure tone audiometric evaluation tests

DoD/OSHA significant threshold shift (STS)	≥10 dB HL threshold shift average shift at 2000, 3000, 4000 Hz
OSHA significant threshold shift age-adjusted	≥10 dB HL threshold shift age-adjusted average shift at 2000, 3000, 4000 Hz
NIOSH material hearing impairment	>25 dB HL threshold average for both ears at 1000, 2000, 3000, 4000 Hz
NIOSH significant threshold shift (NIOSH STS)	≥15 dB HL threshold shift for either ear at any frequency 500, 1000, 2000, 3000, 4000, 6000 Hz
All frequency threshold average	≥25 dB HL threshold average at 500, 1000, 2000, 3000, 4000, 6000 Hz

organize the results into a standard 2×2 format for RR and 95% CI calculation. Air Force Institute of Technology's Human Research Protection Program (HRPP) classified the study as exempt from further review due to the retrospective nature of this research (use of archival data).

RESULTS

Study Population and Exposure Group Characteristics

Similar to the study results reported by Blair et al. (2021), a total of 2372 personnel were organized into eight SEGs with various combinations of exposure to ototoxic substances, impulse noise, and continuous noise. These SEGs were as follows:

- (1) Continuous noise (reference group),
- (2) Continuous noise + Impulse noise,
- (3) Metal exposure + Continuous noise,
- (4) Metal exposure + Continuous noise + Impulse noise,
- (5) Solvent exposure + Continuous noise,
- (6) Solvent exposure + Continuous noise + Impulse noise,
- (7) Metal exposure + Solvent exposure + Continuous noise, and
- (8) Metal exposure + Solvent exposure + Continuous noise + Impulse noise.

As discussed by Blair et al. (2021), the average duration in years between the first audiogram and the final audiogram was approximately 8.7 years (SD 3.1) for the study population. Further analysis of audiogram duration by SEG indicated means and SDs were approximately equal (Blair et al. 2021). Therefore, exposure duration was likely sufficient to demonstrate the gradual hearing loss that occurs within the first 10 years of exposure to occupational noise (Ackley et al. 2007) and the hearing loss that occurs within the first 3–5 years for ototoxicants (Kaufman et al. 2005; Hormozi et al. 2017).

DOEHRS-IH and DOEHRS-HC data are not collected for research purposes. As a result, DOEHRS-HC was not intended to capture audiograms for personnel not entered to a HCP. Therefore, demographics assessed by researchers include only the gender and age distributions of SEGs. Additionally, audiograms were only available for personnel entered to an HCP (rather than a non-noise-exposed population). The study population was 88% male and 12% female with SEG gender demographics predominantly within $\pm 3\%$ of the overall averages (see Table, Supplemental Digital Content 1, <http://links.lww.com/EANDH/A982>). The largest percentage of females in a relatively large-sized exposure group was the continuous noise only group with a 15% female composition. Researchers noted that

the lower representation of female workers could potentially make gender a significant independent variable in inferential statistical analysis.

Researcher analysis of age demographics was conducted by assessing averages of SEGs and categorization of data by age groups. The average age of the total population was 44.7 years (SD 10.2), and each exposure group was approximately similar except for the continuous noise only exposure group having the highest average of 47.3 years averages (see Table, Supplemental Digital Content 2, <http://links.lww.com/EANDH/A982>). Next, researchers grouped values into bins of 10 years to determine the distribution and identified the 38- to 47-year-old age group as the largest of the study population, representing 31% of the total number of workers (see Table, Supplemental Digital Content 3, <http://links.lww.com/EANDH/A982>). Overall, approximately 85% of the study population was between ages 28 and 57 years, and the distribution of ages between SEGs were similar. Comparatively, Masterson et al. (2014) observed 78% of individuals were between the ages of 26- and 55-years old in the evaluation of PTA data, thus supporting the comparison of this study to civilian workers.

Exposure Group Hearing Loss Relative Risks According to PTA Evaluation Method

Researchers assessed the RR of hearing loss indicators using the continuous noise only exposure group as the reference/comparison group. Five PTA evaluation methods were assessed:

- (1) DoD/OSHA STS: ≥10 dB HL threshold shift average shift at 2000, 3000, 4000 Hz,
- (2) OSHA STS age-adjusted: ≥10 dB HL threshold shift age-adjusted average shift at 2000, 3000, 4000 Hz,
- (3) NIOSH STS: ≥15 dB HL threshold shift for either ear at any frequency 500, 1000, 2000, 3000, 4000, 6000 Hz,
- (4) NIOSH material hearing impairment: >25 dB HL threshold average for both ears at 1000, 2000, 3000, 4000 Hz, and
- (5) All Frequency Threshold Average 500–6000 Hz: ≥25 dB HL threshold average at 500, 1000, 2000, 3000, 4000, 6000 Hz.

When PTA evaluation method (1) DoD/OSHA (without age adjustment) STS that considers ≥10 dB HL averaged at 2000, 3000, and 4000 Hz, continuous noise, impulse noise, and ototoxicant SEGs generally had a lower RR than the continuous noise alone SEG but the difference was not statistically significant (Table 3). Using PTA evaluation method (2) OSHA age adjustment STS criteria, every group that included ototoxicant exposure had a $RR > 1$ (RR 1.04 to 1.44) but none were significantly different from STS rates among the continuous noise only reference group (Table 3). However, despite a small group size ($n = 21$), SEG (2) Continuous noise + Impulse noise led to a significantly higher rate of STS development than continuous noise exposure alone with a RR of 3.11, (95% CI, 1.16 to 8.31) (Table 3).

Next, researchers used PTA method (4) NIOSH's "material hearing impairment" criteria, ≥25 dB HL threshold average at 1000, 2000, 3000, 4000 Hz, which allowed researchers to investigate the excess risk of hearing loss in frequencies typically associated with speech discrimination (NIOSH 1998). There were generally lower STS rates for all SEGs; however, SEG (2) Continuous noise + Impulse noise, SEG (5) Solvent exposure + Continuous noise, SEG (7) Metal exposure + Solvent exposure +

TABLE 3. PTA evaluation results

Exposure	Yes STS	No STS	n	RR	CI95L	CI95U
DoD/OSHA STS: ≥ 10 dB HL threshold shift average shift at 2000, 3000, 4000 Hz						
Continuous (reference)	61	249	310	1.0		
Continuous noise + impulse noise	4	17	21	0.97	0.39	2.4
Metal exposure + continuous noise	38	228	266	0.73	0.50	1.05
Metal exposure + continuous noise + impulse noise	1	11	12	0.42	0.06	2.8
Solvent exposure + continuous noise	88	403	491	0.91	0.68	1.22
Solvent exposure + continuous noise + impulse noise	8	40	48	0.85	0.43	1.66
Metal exposure + solvent exposure + continuous noise	152	720	872	0.89	0.68	1.16
Metal exposure + solvent exposure + continuous noise + impulse noise	64	288	352	0.92	0.67	1.27
OSHA age adjustment STS: ≥ 10 dB HL threshold shift average shift at 2000, 3000, 4000 Hz after age adjustment						
Continuous (reference)	19	291	310	1.0		
Continuous noise + impulse noise	4	17	21	*3.11	1.16	8.31
Metal exposure + continuous noise	17	249	266	1.04	0.55	1.96
Metal exposure + continuous noise + impulse noise	0	12	12	0.0		
Solvent exposure + continuous noise	40	451	491	1.33	0.78	2.25
Solvent exposure + continuous noise + impulse noise	4	44	48	1.36	0.48	3.83
Metal exposure + solvent exposure + continuous noise	57	815	872	1.07	0.65	1.76
Metal exposure + solvent exposure + continuous noise + impulse noise	31	321	352	1.44	0.83	2.49
NIOSH material hearing impairment: >25 dB HL threshold average for both ears at 1000, 2000, 3000, 4000 Hz						
Continuous (reference)	14	296	310	1.0		
Continuous noise + impulse noise	3	18	21	3.16	0.99	10.15
Metal exposure + continuous noise	9	257	266	0.75	0.33	1.7
Metal exposure + continuous noise + impulse noise	0	12	12	0.0		
Solvent exposure + continuous noise	24	467	491	1.08	0.57	2.06
Solvent exposure + continuous noise + impulse noise	1	47	48	0.46	0.06	3.43
Metal exposure + solvent exposure + continuous noise	40	832	872	1.02	0.56	1.84
Metal exposure + solvent exposure + continuous noise + impulse noise	25	327	352	1.57	0.83	2.97
500-6000 Hz frequency average (≥ 25 dB HL): ≥ 25 dB HL threshold average at 500, 1000, 2000, 3000, 4000, 6000 Hz						
Continuous (reference)	16	294	310	1.0		
Continuous noise + impulse noise	2	19	21	1.85	0.45	7.5
Metal exposure + continuous noise	9	257	266	0.66	0.29	1.46
Metal exposure + continuous noise + impulse noise	1	11	12	1.61	0.23	11.19
Solvent exposure + continuous noise	26	465	491	1.03	0.56	1.88
Solvent exposure + continuous noise + impulse noise	1	47	48	0.4	0.05	2.97
Metal exposure + solvent exposure + continuous noise	40	832	872	0.89	0.51	1.56
Metal exposure + solvent exposure + continuous noise + impulse noise	22	330	352	1.21	0.65	2.26
NIOSH STS: ≥ 15 dB HL threshold shift for either ear at any frequency 500, 1000, 2000, 3000, 4000, 6000 Hz						
Continuous (reference)	173	137	310	1.0		
Continuous noise + impulse noise	9	12	21	0.77	0.46	1.27
Metal exposure + continuous noise	154	112	266	1.04	0.9	1.2
Metal exposure + continuous noise + impulse noise	6	6	12	0.9	0.5	1.59
Solvent exposure + continuous noise	281	210	491	1.03	0.9	1.16
Solvent exposure + continuous noise + impulse noise	29	19	48	1.08	0.84	1.39
Metal exposure + solvent exposure + continuous noise	493	379	872	1.01	0.9	1.14
Metal exposure + solvent exposure + continuous noise + impulse noise	220	132	352	1.12	0.99	1.27

*Significantly greater RR than the reference group.

RR, relative risk; CI95L/U, confidence interval 95% lower/upper.

Continuous noise, and SEG (8) Metal exposure + Solvent exposure + Continuous noise + Impulse noise all had $RR > 1$. STS rates for SEG (2) Continuous noise + Impulse noise in combination was the group closest to being significantly different than SEG (1) Continuous noise reference group with a RR 3.16 (95% CI, 0.99 to 10.15); however, none of the SEGs were significantly different than SEG (1) Continuous noise reference group.

When assessing PTA results with method (5), All Frequency Threshold Average evaluation, and similar to the other PTA evaluation techniques, SEG (2) Continuous noise + Impulse noise had the highest RR at 1.85 (95% CI, 0.45 to 7.5) followed

by SEG (4) Metal exposure + Continuous noise + Impulse noise with a RR of 1.61 (95% CI, 0.23 to 11.19) and SEG (8) Metal exposure + Solvent exposure + Continuous noise + Impulse noise with an RR of 1.21 (95% CI, 0.65 to 2.26). Despite these elevated RR s, no exposure group had significantly different hearing thresholds compared to SEG (1) continuous noise reference group.

In contrast, RR s > 1 were found for nearly all SEGs with an ototoxicant exposure component when using PTA method (3) NIOSH STS criteria. Specifically, SEG (3) Metal exposure + Continuous noise with a RR of 1.04 (95% CI, 0.90 to 1.20),

SEG (5) Solvent exposure + Continuous noise with an RR of 1.03 (95% CI, 0.9 to 1.16), SEG (7) Metal exposure + Solvent exposure + Continuous noise with a RR of 1.01 (95% CI, 0.90 to 1.14), and SEG (8) Metal exposure + Solvent exposure + Continuous noise + Impulse noise with a RR of 1.12 (95% CI, 0.99 to 1.27) had more narrow CIs that nearly reached significant difference levels compared to the reference group. While these results revealed the relative risk was not significantly higher than the continuous noise only group, results suggest the addition of ototoxicants increases the risk of developing a NIOSH STS (PTA evaluation method 3).

DISCUSSION

Researchers used various PTA evaluation methods for personnel exposed to various combinations of continuous noise, impulse noise, and ototoxicants. This approach was warranted because the differing frequencies and mathematical functions used in each PTA evaluation method could potentially alter indication of hearing loss development rates. In particular, PTA evaluation methods typically do not group low (500 to 1000 Hz) with high frequencies (6000 Hz). For example, the usage of only the DoD/OSHA STS criteria (method 1), which defines an average threshold shift across 2000, 3000, and 4000 Hz, may not accurately describe the health effects from ototoxic substances that impact the 500, 1000, or 6000 Hz octave bands. Thus, the assessment of multiple PTA evaluation methods was necessary to evaluate changes in hearing thresholds over several frequencies and identify the optimal method for evaluating exposures to continuous noise, impulse noise, and ototoxic substances.

Researchers adjusted PTA data consistent with OSHA age adjustment criteria (method 2) to determine whether age was a potential confounding factor in the development of hearing loss. As observed in the OSHA age adjustment STS method (2), where ototoxicants were a component of exposure, SEG (5) Solvent exposure + Continuous noise RR 1.33, (95% CI, 0.78 to 2.25), SEG (8) Metal exposure + Solvent exposure + Continuous noise + Impulse noise RR 1.44, (95% CI, 0.83 to 2.49), and SEG (6) Solvent exposure + Continuous noise + Impulse noise exposure group RR 1.36, (95% CI, 0.48 to 3.83) continued to demonstrate the highest RRs for an age-adjusted STS despite not being significantly different than the reference group. Researchers observed the rates of hearing loss after age adjustment ($19/310 = 6.1\%$) were similar to the approximately 6.4% prevalence observed by Masterson et al. (2014) in assessing industries by NAICS. Despite disagreements on the application of age adjustments in literature and by NIOSH (1998), results suggest ototoxic exposures may increase hearing loss rates when accounting for age variables.

As shown in Table 3, results of the current investigation also suggest hearing impairment due to continuous noise and impulse noise primarily occurs at 1000 to 4000 Hz with RRs in SEG (2) Continuous noise + Impulse noise ranging from 3.11 (OSHA age adjustment method 2) to 3.16 (NIOSH Material Hearing Impairment method 4). The combined risk of developing an STS from continuous and impulse noise exposure being over three times continuous noise exposure alone suggests the combined influence of the two types of noise may be better observed with OSHA Age Adjusted (method 2) and NIOSH Material Hearing Impairment PTA (method 4) evaluation methods rather than the 500 to 6000 Hz full frequency

averaging PTA (method 5) and NIOSH STS (method 3) evaluation method.

In addition, the researchers found RRs > 1 at near significant increased STS rates for nearly all SEGs with an ototoxicant exposure component, and narrow CIs when evaluating PTAs with the NIOSH STS criteria. This was specifically true for SEG (8) Metal exposure + Solvent exposure + Continuous noise + Impulse noise exposure group. Researchers' postulated NIOSH STS evaluation (method 3) is potentially more sensitive in the evaluation of ototoxic effects because of the inclusion of the 500, 1000, and 6000 Hz frequencies (compared to other PTA evaluation methods that omit these frequencies) and the usage of absolute shifts by independent frequency instead of averaging values. These results are consistent with Schaal et al. (2018) who found significantly higher levels of hearing loss when considering dB HL at 500 to 6000 Hz in an industrial workforce due to exposure to ototoxicants such as lead, cadmium, and arsenic at OSHA Action Levels and ototoxicants such as toluene and xylene at sub-OEL concentrations. Chang et al. (2006) found similar results due to combined toluene and noise exposure that increased hearing thresholds at 1000 and 2000 Hz. Fuente et al. (2018) similarly found significant hearing changes due to impulse noise and solvents at 6000 Hz. These results suggest the more conservative NIOSH STS (method 3) PTA evaluation technique of ≥ 15 dB HL at any frequency from 500, 1000, 2000, 3000, 4000, 6000 Hz is more sensitive in detecting hearing changes due to ototoxicants above and beyond the hearing damage from only continuous noise.

The variety of methods to determine threshold shifts can lead to challenges in comparing and interpreting the results of HCP assessments or assessing excess risk from other occupational exposures. A key concern for the current investigation along with similar studies relying on retrospective hearing assessment is that PTA data exists primarily due to the requirement for personnel entry in an HCP for such reasons as exposure above an 8-hour TWA of 85 dBA. Differing methods of evaluating PTA results may lead to various conclusions when identifying hearing loss.

Because in the current study no PTA method revealed a significantly greater RR for hearing loss in SEGs that included ototoxicants compared to the reference group, it is possible that PTA is not appropriate for detecting hearing loss associated with ototoxicants. PTA is a common element of an HCP but several other methods of hearing evaluation are available and typically used as follow-on tests to PTA. These include speech audiometry, auditory brainstem response (ABR), distortion product otoacoustic emissions (DPOAEs), and slow vertex potential (SVP). In speech audiometry, tests utilizing spoken or recorded voices provide a method to assess awareness, discrimination, and identification/recognition (Roeser et al. 2000). ABR, a component of auditory-evoked potentials, measures the electrical activity of a series of seven waves that occur within 10 ms of stimulus to detect damage to the auditory nerve and brainstem (Roeser et al. 2000). DPOAE evaluate the results of a stimulus to detect hair cell abnormalities by monitoring the evoked and spontaneous otoacoustic emissions (Roeser et al. 2000). In an investigation by Guthrie et al. (2016), to determine the effect of repeated exposure to low intensity noise with and without exposure to an organic solvent blend using ABR, DPOAE, and SVPs, subtoxic solvent exposure alone had no statistically significant effects. However, background noise significantly suppressed brain

activity and slowed neurotransmission, which was exacerbated with solvent exposure and occurred in the absence of hearing loss and detectable damage to sensory cells. The adverse effects on brain activity and neurotransmission may lead to poor speech recognition, reduced speed of signal processing within the auditory pathways, and reduced cognition, which may have a detrimental effect on worker quality of life. Despite other tests beyond PTA, such as ABR, DPOAE, and SVPs, potentially capable of detecting adverse hearing effects from ototoxicants and noise, PTA was the only auditory outcome available for analysis in DOEHS-HC. Additionally, use of tests other than PTA is rarely used as a component of an HCP for the DoD.

Despite the large sample size of this retrospective cohort study as a whole ($n = 2372$), three of the eight SEGs had small sample sizes and low rates of hearing loss development, which resulted in a broad CI range. Like most retrospective cohort studies where exposure groups may not be equal in size or some exposure combinations may not be represented, investigators used the best data available in DOEHS-IH and DOEHS-HC. Other studies designed similarly as ours and relying on DOEHS data had similar SEG size characteristics. The results of Soderlund et al. (2016) investigating prevalence of permanent threshold shifts using PTAs were skewed by the small numbers in different career field classifications and due to low hearing loss prevalence. An investigation by Hughes and Hunting (2013) investigating the effects of organic solvents and noise on hearing had similar issues with only 503 subjects and four groups. These studies showed that (1) DOEHS includes useful data and can be used to address research questions and (2) other studies with small group numbers may still be used to form conclusions.

Additionally, no non-noise-exposed reference group was available for this study. The connection between noise and hearing loss is well recognized but the addition of other risk factors combined with continuous noise has not been investigated thoroughly in the past. With this understanding, our research objective was to determine the relative risks of hearing impairment from co-exposure to continuous noise, impulse noise, metal ototoxicants, and solvent ototoxicants compared to the already well-known hearing impairment risk presented by only continuous noise. Additionally, the DoD HCP model is similar to OSHA's where noise exposure is needed to require PTAs. If there is no noise exposure then PTAs would not be required and would likely not have been accomplished. We do admit caution with drawing conclusions from small groups but the overall study was relatively large and the results of the current investigation address our original research objective and suggests that using a single NIHL definition may not be suitable to detect hearing changes when a complex set of hazards are present (physical, chemical, pharmaceutical). Additionally, use of multiple standard threshold shift definitions highlight different possible effects based on exposure group. Future research planned by this research team will assess similar conditions but for multiple maintenance facilities across the U.S. Air Force, which is anticipated to provide a larger group sample size.

LIMITATIONS

As discussed in detail by Blair et al. (2021), there were limitations of the current study. Not every occupational hazard that contributes to hearing impairment was sampled/quantified for

both ototoxicant chemicals and impulse noise and, as a result, dichotomous exposure classifications were developed instead of determination of dose-response relationships. This limitation also prevented determining specific contributions of each respective ototoxic metal and solvent in contributing to the RR of STS development and dB HL overall. Demographic data from DOEHS-IH and DOEHS-HC were limited to age and gender. As a result, this investigation was unable to account for confounding factors of hearing loss that could include personal usage of firearms, recreational activities involving ototoxicant and noise exposures, smoking, alcohol usage, or ototoxic pharmaceutical usage. However, this potential confounding was expected to be nondifferential between SEGs. Despite these limitations, this study contributed to an understudied area by targeting combinations of metals, solvents, and noise exposures on hearing loss and focusing on several PTA evaluation techniques. Additionally, this investigation included a large sample size during a lengthy 14-year duration consistent with the chronic nature of exposure effects associated with solvents, metals, and noise.

CONCLUSIONS

Researchers investigated various PTA evaluation methods to identify the optimal criteria for determining adverse hearing health effects from combined exposures to continuous noise, impulse noise and ototoxic substances. None of the continuous noise, impulse noise, and ototoxicant SEGs had significantly greater levels of hearing loss compared to a continuous noise alone reference group using the various PTA evaluation methods. However, the NIOSH STS evaluation method (method 3) appeared to be the most sensitive method for observing ototoxicant effects due to inclusion of all frequencies from 500 to 6000 Hz and a lack of averaging functions applicable to other PTA evaluation methods. Additionally, while not a central focus of the current investigation, hearing impairment due to continuous noise and impulse noise primarily occurring at 1000 to 4000 Hz suggests the combined influence of continuous noise and impulse noise may be better observed with DoD/OSHA (method 1), OSHA Age Adjusted (method 2), and NIOSH Material Hearing Impairment (method 4) PTA evaluation methods rather than the 500 to 6000 Hz full frequency averaging PTA (method 5) and NIOSH STS (method 3) evaluation method.

While this investigation was not able to study exposures to individual stressors to determine their level of influence in leading to hearing loss, exposure combinations beyond just continuous noise exposure in many workplace environments are common and appear to influence hearing loss. This investigation's results suggest that a single PTA evaluation technique may not be adequate in fully revealing hearing impairment risk due to all stressors and rather, tailoring the PTA evaluation technique to the hazards present in the workplace could better detect hearing impairment. Additionally, results suggest that PTA may not be effective as the sole technique for evaluating hearing impairment due to ototoxicant exposure.

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